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=> d his

     (FILE 'HOME' ENTERED AT 12:06:32 ON 30 MAY 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 12:06:50 ON 30 MAY
     2003
L1         46839 S (ADENOVIR? OR AD)(4A)(2 OR 3 OR 5 OR 11 OR 16 OR 31 OR 21 OR
L2           279 S ADENOVIRUS(4A)(SUBGROUP OR GROUP)(W)(A OR B OR C)
L3         46923 S L1 OR L2
L4         32704 S (INFECT? OR TROPISM)(5A)(ENDOTHELIAL OR LIVER OR HEPATIC OR H
L5           273 S L3 AND L4
L6           140 S L3(S)L4
L7            76 DUP REM L6 (64 DUPLICATES REMOVED)
L8           469 S (REDUC? OR DECREAS?)(3A)(INFECT? OR TROPISM)(4A)(LIVER OR HEP
L9           129 S (INCREAS? OR ENHANC? OR IMPROV?)(3A)(INFECT? OR TROPISM)(5A)(
L10          598 S L8 OR L9
L11           16 S L3 AND L10
L12            9 DUP REM L11 (7 DUPLICATES REMOVED)

=> d bib ab 1-9 l12

L12  ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2003 ACS
AN   2003:42418  CAPLUS
DN   138:84482
TI   Adenoviral gene delivery vectors with cell type specificity for
     mesenchymal stem cells and therapeutic uses
IN   Havenga Menzo, Jans Emco; Bout, Abraham; Vogels, Ronald
PA   Crucell Holland B.V., Neth.
SO   PCT Int. Appl., 63 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.         KIND  DATE            APPLICATION NO.   DATE
     ---------------    ----  --------        ---------------   --------
PI   WO 2003004661      A2    20030116        WO 2002-NL443     20020705
         W:  AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES,
             FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,
             KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
             MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK,
             SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW,
             AM, AZ, BY, KG
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
     EP 1279738          A1    20030129        EP 2001-202619    20010706
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRAI EP 2001-202619     A     20010706
     US 2001-303734P    P     20010707
     US 2001-10645      A     20011113
AB   The present invention provides novel methods and means for delivering a
     heterologous nucleic acid of interest to mesenchymal stem cells by
     providing recombinant adenoviral vectors provided with, or having a
     natural tropism for mesenchymal stem cells, typically in combination with
     a reduced tropism for other kinds of cells, in particular liver cells.
     The invention also provides mesenchymal stem cells provided with a
     heterologous nucleic acid through the use of a recombinant adenoviral
     vector according to the invention, and the use of such mesenchymal stem
     cells for the prepn. of medicaments for the treatment of multiple
     sclerosis, rheumatoid arthritis, angiogenesis and bone related disorders,
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for instance in treatments that involve bone (re)generation.

L12 ANSWER 2 OF 9 MEDLINE DUPLICATE 1
AN 2003042985 MEDLINE
DN 22440018 PubMed ID: 12551989
TI **Reduction** of natural adenovirus **tropism** to the **liver** by both ablation of fiber-coxsackievirus and adenovirus receptor interaction and use of replaceable short fiber.
AU Nakamura Takafumi; Sato Kenzo; Hamada Hirofumi
CS Department of Molecular Medicine, Sapporo Medical University, S1 W17, Chuo-ku, Sapporo 060-8556, Japan.. Nakamura.Takafumi@mayo.edu
SO JOURNAL OF VIROLOGY, (2003 Feb) 77 (4) 2512-21.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200303
ED Entered STN: 20030129
Last Updated on STN: 20030316
Entered Medline: 20030314
AB The initial recognition and binding of adenovirus vector to the host cell surface is mediated by interaction between the adenovirus fiber knob protein and its receptor, the coxsackievirus and adenovirus receptor (CAR). This natural tropism of adenovirus vector needs to be ablated in order to achieve targeted gene transfer. To this end, we noted that adenovirus serotype 40 (Ad40) contains two distinct long and short fibers; the short fiber is unable to recognize CAR, while the long fiber binds CAR. We generated **adenovirus** serotype **5**-based mutants with chimeric Ad40-derived fibers, which were composed of either long or short shafts together with CAR binding or nonbinding knobs. The capacity of these adenovirus mutants for in vitro and in vivo gene transfer to liver cells was examined. In the case of primary human hepatocytes displaying a high expression level of CAR and alphav integrin, both CAR binding ability and fiber shaft length played important roles in efficient transduction. Most significantly, the high transduction efficiency observed in the liver and spleen following intravenous administration of adenovirus vector was dramatically reduced by both ablation of fiber-CAR interaction and the use of replaceable short fiber. In other tissues displaying a low level of transduction, no significant differences in transduction efficiency were observed among adenovirus vector mutants. Furthermore, incorporation of a 7-lysine-residue motif at the C-terminal end of CAR-nonbinding short fiber efficiently achieved transduction of target cells via the heparan-containing receptor. Our results demonstrated that the natural tropism of adenovirus in vivo is influenced not only by fiber-CAR interaction but also by fiber shaft length. Furthermore, our strategy may be useful for retargeting adenovirus to particular tumors and tissue types with specific receptors.

L12 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2003 ACS
AN 2002:310703 CAPLUS
DN 137:198842
TI Maintaining HNF6 expression prevents AdHNF3.beta.-mediated decrease in hepatic levels of Glut-2 and glycogen
AU Tan, Yongjun; Adami, Guy; Costa, Robert H.
CS Department of Molecular Genetics, College of Medicine, University of Illinois at Chicago, Chicago, IL, 60607-7170, USA
SO Hepatology (Philadelphia, PA, United States) (2002), 35(4), 790-798
CODEN: HPTLD9; ISSN: 0270-9139
PB W. B. Saunders Co.
DT Journal
LA English
AB The hepatocyte nuclear factor 3 (HNF-3) proteins are members of the Forkhead Box (Fox) family of transcription factors that play important

roles in regulating expression of genes involved in cellular proliferation, differentiation, and metabolic homeostasis. In previous studies we increased liver expression of HNF-3.beta. by using either transgenic mice (transthyretin HNF-**3**.beta.) or recombinant **adenovirus** infection (AdHNF3.beta.), and obsd. diminished hepatic levels of glycogen, and glucose transporter 2 (Glut-2), as well as the HNF-6, HNF-3, HNF-1.alpha., HNF-4.alpha., and C/EBP.alpha. transcription factors. We conducted the present study to det. whether maintaining HNF-6 protein expression during AdHNF3.beta. **infection** prevents **redn**. of **hepatic** levels of glycogen and the earlier-mentioned genes. Here, we show that AdHNF3.beta.- and AdHNF6-infected mouse liver displayed increased hepatic levels of glycogen, Glut-2, HNF-3.gamma., HNF-1.alpha., and HNF-4.alpha. at 2 and 3 days postinfection (PI). Furthermore, restoration of hepatic glycogen levels after AdHNF3.beta. and AdHNF6 coinfection was assocd. with increased Glut-2 expression. AdHNF6 infection alone caused a 2-fold increase in hepatic Glut-2 levels, suggesting that HNF 6 stimulates in vivo transcription of the Glut-2 gene. DNA binding assays showed that only recombinant HNF-6 protein, but not the HNF-3 proteins, binds to the mouse -185 to -144 bp Glut-2 promoter sequences. Cotransfection assays in human hepatoma (HepG2) cells with either HNF-3 or HNF-6 expression vectors show that only HNF-6 provided significant transcriptional activation of the Glut-2 promoter. In conclusion, these studies show that the hepatic Glut-2 promoter is a direct target for HNF-6 transcriptional activation.

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2003 ACS
AN 2002:674871 CAPLUS
DN 138:231527
TI Peptide-retargeted adenovirus encoding a tissue inhibitor of metalloproteinase-1 decreases restenosis after intravascular gene transfer
AU Turunen, Mikko P.; Puhakka, Hanna L.; Koponen, Jonna K.; Hiltunen, Mikko O.; Rutanen, Juha; Leppanen, Olli; Turunen, Anna-Mari; Narvanen, Ale; Newby, Andrew C.; Baker, Andrew H.; Yla-Herttuala, Seppo
CS A.I. Virtanen Institute, University of Kuopio, Kuopio, Finland
SO Molecular Therapy (2002), 6(3), 306-312
CODEN: MTOHCK; ISSN: 1525-0016
PB Elsevier Science
DT Journal
LA English
AB In this study we have attached cyclic targeting peptides by way of a poly-lysine spacer on the surface of an adenovirus using a transglutaminase enzymic reaction to enhance transduction efficiency and to modify tissue tropism in vivo. Nuclear targeted lacZ- and TIMP-1-encoding adenoviruses were coupled to a peptide-motif (HWGF) that can bind to matrix metalloproteinase (MMP)-2 and MMP-9. Modified viruses were used to evaluate gene transfer efficiency, biodistribution, and the effect on neointima formation following balloon denudation injury. In vitro, both rabbit aortic smooth muscle cells and human endothelial hybridoma cells demonstrated significantly increased reporter gene expression with HWGF-modified adenoviruses (AdlacZ(HWGF)) compared with control (AdlacZ) or mismatch peptide-modified (AdlacZ(MM)) adenoviruses. However, in human hepatocellular Hep-G2 cells, both AdlacZ(HWGF) and AdlacZ(MM) produced significantly lower transgene expression compared with the resp. control viruses. In vivo, local intravascular catheter-mediated gene transfer of a HWGF-targeted TIMP-1-encoding adenovirus (AdTIMP-1(HWGF)) significantly reduced intimal thickening in a rabbit aortic balloon denudation model ($P < 0.05$) compared with the control adenovirus. X-Gal staining and biodistribution analyses with TaqMan RT-PCR revealed that the cyclic peptides altered vector **tropism** and, in particular, **reduced** transduction of the **liver**. We found that the HWGF peptide modification increased transduction efficiency of the adenovirus-mediated gene transfer in smooth muscle cells

and endothelial cells in in vitro and enhanced gene transfer to the arterial wall in vivo; that peptide modification of adenoviruses beneficially modulated tissue tropism in vivo; and that efficient TIMP-1 gene transfer reduced intimal thickening in an established restenosis model in rabbits.

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2003 ACS
AN 2001:50835 CAPLUS
DN 134:126789
TI Infection with chimeric adenoviruses of cells negative for the **adenovirus** serotype **5** coxsackie **adenovirus** receptor (CAR)
IN Havenga, Menzo; Vogels, Ronald
PA Introgene B.V., Neth.; Crucell Holland B.V.
SO PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001004334	A2	20010118	WO 2000-NL481	20000707
	WO 2001004334	A3	20010705		
	WO 2001004334	C2	20020906		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1067188	A1	20010110	EP 1999-202234	19990708
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	EP 1196594	A2	20020417	EP 2000-946537	20000707
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 2003096415	A1	20030522	US 2002-40949	20020107
PRAI	US 1999-142557P	P	19990707		
	EP 1999-202234	A	19990708		
	WO 2000-NL481	W	20000707		

AB The invention discloses a method for delivering a nucleic acid of interest to a host cell by means of a gene delivery vehicle based on adenoviral material. One of the problems assocd. with the development of effective gene therapy protocols for the treatment of disease is the limitation of the current vectors to effectively transduce cells in vivo. This problem is overcome with chimeric adenoviruses comprising capsids derived from **adenovirus 5** of which at least part of the **adenovirus 5** fiber protein is replaced by a fiber protein from a different adenovirus serotype. The gene delivery vehicle delivers a nucleic acid to the host cell by assocg. with a binding site and/or a receptor present on CAR-neg. cells, said binding site and/or receptor being a binding site and/or a receptor for adenovirus subgroups D and/or F. For this purpose, two or three plasmids, which together contain the complete **adenovirus** serotype **5** genome, were constructed. From a plasmid the DNA encoding the **adenovirus** serotype **5** fiber protein is essentially removed and replaced by linker DNA sequences which facilitate easy cloning. This plasmid subsequently serves as template for the insertion of DNA encoding the fiber protein derived from different adenovirus serotypes. At the former

E1 location in the genome of **adenovirus** serotype **5**, any gene of interest can be cloned. A single transfection procedure of the two or three plasmids together result in the formation of a recombinant chimeric adenovirus. The invention also describes the construction and use of plasmids consisting of distinct parts of **adenovirus** serotype **5** in which the gene encoding for fiber protein has been replaced with DNA derived from alternative human or animal serotypes.

L12 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2003 ACS
AN 2001:28651 CAPLUS
DN 134:111233
TI Infection with chimeric adenoviruses of cells negative for the **adenovirus** serotype **5** coxsackie **adenovirus** receptor (CAR)
IN Havenga, Menzo; Vogels, Ronald
PA Introgene B.V., Neth.
SO Eur. Pat. Appl., 95 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1067188	A1	20010110	EP 1999-202234	19990708
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	WO 2001004334	A2	20010118	WO 2000-NL481	20000707
	WO 2001004334	A3	20010705		
	WO 2001004334	C2	20020906		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1196594	A2	20020417	EP 2000-946537	20000707
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI	US 1999-142557P	P	19990707		
	EP 1999-202234	A	19990708		
	WO 2000-NL481	W	20000707		

AB The invention discloses a method for delivering a nucleic acid of interest to a host cell by means of a gene delivery vehicle based on adenoviral material. One of the problems assocd. with the development of effective gene therapy protocols for the treatment of disease is the limitation of the current vectors to effectively transduce cells in vivo. This problem is overcome with chimeric adenoviruses comprising capsids derived from **adenovirus 5** of which at least part of the **adenovirus 5** fiber protein is replaced by a fiber protein from a different adenovirus serotype. The gene delivery vehicle delivers a nucleic acid to the host cell by assocg. with a binding site and/or a receptor present on CAR-neg. cells, said binding site and/or receptor being a binding site and/or a receptor for adenovirus subgroups D and/or F. For this purpose, two or three plasmids, which together contain the complete **adenovirus** serotype **5** genome, were constructed. From a plasmid the DNA encoding the **adenovirus** serotype **5** fiber protein is essentially removed and replaced by linker DNA sequences which facilitate easy cloning. This plasmid subsequently serves as template for the insertion of DNA encoding the fiber protein derived from different adenovirus serotypes. At the former

E1 location in the genome of **adenovirus** serotype **5**, any gene of interest can be cloned. A single transfection procedure of the two or three plasmids together result in the formation of a recombinant chimeric adenovirus. The invention also describes the construction and use of plasmids consisting of distinct parts of **adenovirus** serotype **5** in which the gene encoding for fiber protein has been replaced with DNA derived from alternative human or animal serotypes.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2003 ACS
AN 2001:832874 CAPLUS
DN 136:320013
TI Reducing the native tropism of adenovirus vectors requires removal of both CAR and integrin interactions
AU Einfeld, David A.; Schroeder, Rosanna; Roelvink, Peter W.; Lizonova, Alena; King, C. Richter; Kovesdi, Imre; Wickham, Thomas J.
CS GenVec, Inc., Gaithersburg, MD, 20878, USA
SO Journal of Virology (2001), 75(23), 11284-11291
CODEN: JOVIAM; ISSN: 0022-538X
PB American Society for Microbiology
DT Journal
LA English
AB The development of tissue-selective virus-based vectors requires a better understanding of the role of receptors in gene transfer in vivo, both to rid the vectors of their native tropism and to introduce new specificity. CAR and .alpha.v integrins have been identified as the primary cell surface components that interact with **adenovirus** type **5** (Ad5)-based vectors during in vitro transduction. We have constructed a set of four vectors, which individually retain the wild-type cell interactions, lack CAR binding, lack .alpha.v integrin binding, or lack both CAR and .alpha.v integrin binding. These vectors have been used to examine the roles of CAR and .alpha.v integrin in detg. the tropism of Ad vectors in a mouse model following intrajugular or i.m. injection. CAR was found to play a significant role in liver transduction. The absence of CAR binding alone, however, had little effect on the low level of expression from Ad in other tissues. Binding of .alpha.v integrins appeared to have more influence than did binding of CAR in promoting the expression in these tissues and was also found to be important in liver transduction by Ad vectors. An effect of the penton base modification was a redn. in the no. of vector genomes that could be detected in several tissues. In the liver, where CAR binding is important, combining defects in CAR and .alpha.v integrin binding was essential to effectively reduce the high level of expression from Ad vectors. While there may be differences in Ad vector tropism among species, our results indicate that both CAR and .alpha.v integrins can impact vector distribution in vivo. Disruption of both CAR and .alpha.v integrin interactions may be crit. for effectively reducing native tropism and enhancing the efficacy of specific targeting ligands in redirecting Ad vectors to target tissues.

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 9 MEDLINE DUPLICATE 2
AN 2000186607 MEDLINE
DN 20186607 PubMed ID: 10724040
TI Liver bypass significantly increases the transduction efficiency of recombinant adenoviral vectors in the lung, intestine, and kidney.
AU Ye X; Jerebtsova M; Ray P E
CS Center for Genetic Medicine Research, Children's Research Institute, Children's National Medical Center, Washington, DC 20010, USA.. xye@cnmc.org
NC HL55606 (NHLBI)
SO HUMAN GENE THERAPY, (2000 Mar 1) 11 (4) 621-7.

Journal code: 9008950. ISSN: 1043-0342.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200004
ED Entered STN: 20000421
Last Updated on STN: 20000421
Entered Medline: 20000413
AB Recombinant adenoviruses have great potential as gene delivery systems because of their ability to infect a wide range of target cells. However, systemic delivery of viral vectors to tissues other than liver and spleen has been inefficient because of the rapid clearance of the circulating virus by the liver. In the present study we tested the hypothesis that a systemic administration of E1-deleted recombinant adenovirus vectors that bypasses the hepatic circulation will lead to enhanced expression of these vectors in extrahepatic tissues. The portal vein and hepatic artery in B6/129 F1 mice were clamped and an E1-deleted recombinant adenovirus carrying the beta-galactosidase gene (Ad.CBlacZ) was then administered through the retroorbital venous plexus. The clamp was released 30 min after viral injection with no major chronic ischemic consequences noted. High levels of LacZ expression were detected predominantly in the vessels and capillaries of the lung, intestinal wall, and renal glomeruli 7 days after viral infusion. The transgene expression persisted for at least 21 days. Intense LacZ staining was also observed in the liver, suggesting that liver infection occurred after the portal clamp was released. A retroorbital infusion of anti-**adenovirus** neutralizing antibodies **5** min before the release of the portal clamp significantly **reduced** postclamp viral **infection** to the **liver**, while LacZ expression in lung and intestine persisted after the antibody treatment. Taken together, these results suggest that liver bypass can significantly improve the transduction efficiency in the other target organs. This method could be used to develop animal models of human diseases that predominantly affect the vessels of the lung, intestine, and kidney.

L12 ANSWER 9 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
AN 2000:408596 BIOSIS
DN PREV200000408596
TI Induction of cyclooxygenase-2 by overexpression of the human catalase gene in cerebral microvascular endothelial cells.
AU Fang, Xiang (1); Moore, Steven A.; Nwankwo, Joseph O.; Weintraub, Neal L.; Oberley, Larry W.; Snyder, Gary D.; Spectro, Arthur A.
CS (1) Department of Biochemistry, University of Iowa, 4-403 BSB, Iowa City, IA, 52242 USA
SO Journal of Neurochemistry, (August, 2000) Vol. 75, No. 2, pp. 614-623. print.
ISSN: 0022-3042.
DT Article
LA English
SL English
AB Prostaglandin (PG) formation by the inducible (type 2) cyclooxygenase (COX-2) and reactive oxygen species (ROS) have been proposed to play important roles in cerebrovascular pathological processes. To explore the relationship between ROS and COX-**2** expression, **adenovirus** (**Ad**) vectors containing cDNA for human antioxidant enzymes including catalase (AdCat), copper/zinc superoxide dismutase (AdCu/ZnSOD), and manganese superoxide dismutase (AdMnSOD) were transferred into murine cerebral microvascular **endothelial** cells. AdCat (100 multiplicity of **infection**) infection **increased** the content and enzymatic activity of cellular Cat threefold and decreased the intracellular peroxide level. The expression of COX-2 mRNA and protein in cell lysates was up-regulated, and the amount of PGE2 formed from exogenous arachidonic acid increased following AdCat

infection in a dose-dependent manner, paralleling the expression of COX-2 protein. The AdCat-induced increase in PGE2 formation was inhibited by NS-398, a selective inhibitor of COX-2 enzymatic activity. AdCat infection did not change the expression of the constitutive (type 1) COX protein. Although AdCu/ZnSOD and AdMnSOD infection increased the expression of superoxide dismutase proteins, COX-2 expression was not induced. An in vitro nuclear transcription assay indicated that overexpression of the Cat gene increases the transcription of the COX-2 gene. Furthermore, the stability of COX-2 mRNA induced by lipopolysaccharide was increased after AdCat gene transfer. These results indicate that AdCat gene transfer induces the transcriptional activation of the COX-2 gene and increases COX-2 mRNA stability. Therefore, peroxide may have regulatory effect on COX-2 function in the cerebral microcirculation.

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